

## REMARKS

### Objection to the drawings

The Examiner objected to the drawings under 37 CFR 1.83(a), stating that the drawings must show every feature of the invention specified in the claims. Applicants respectfully request clarification of the objection. It is unclear to the Applicants whether the Examiner is requesting additional drawings or changes to the present drawings. The drawings that were originally filed were not intended to illustrate the device, but rather are graphical representations to demonstrate that GFP and CAT are successfully translated in a multi-well apparatus of the present invention. Under 37 CFR 1.81(a), drawings only need to be submitted when they are necessary for the understanding of the subject matter. Applicants do not believe that further drawings are necessary for the present invention, which is fully supported and enabled by the written specification as it currently stands. The Applicants request clarification: is the Examiner requesting drawings under 37 CFR 1.81(c)? Or is the Examiner requesting some modification of the drawings originally submitted?

### Rejections based upon 35 USC §112, second paragraph

Citing 35 USC §112, second paragraph, the Examiner rejected claims 16-30, stating that claim 16 (and therefore the claims dependent thereon) was indefinite because it was unclear if “a semipermeable membrane” as recited in line 12 is the same or different from that recited in line 10. Applicants have submitted an amended claim 16 that rectifies this confusion.

The Examiner also rejected claims 29 and 30 as indefinite, stating that these claims fail to positively recite method steps. Applicants have amended claims 29 and 30 to rectify this error. Applicants respectfully request that the rejections based upon §112 be withdrawn based upon the amendments to the claims.

### Rejection based upon 35 USC §102(b)

The Examiner rejected claims 16, 17, 24, 25, 27, and 28 as being anticipated by Medicus et al. Applicants respectfully disagree with this rejection. Claim 16 as originally submitted clearly requires that the wells of the inner housing contain a producing system. The Medicus reference deals only with a device for dialysis, and there is no mention of a producing system. For this reason, the Medicus reference is missing a required element of claim 16 (and therefore

all claims dependent thereon) and cannot properly be cited as a §102 reference. Applicants respectfully request that this rejection be withdrawn.

Rejections based upon 35 USC §103

Paragraph 11: Claims 21 and 22 stand rejected under §103(a) as obvious over Medicus et al. As described above, the Medicus reference fails to disclose a producing system, and fails to teach that the system disclosed therein is adaptable to any purpose for producing peptides or running biological reactions. Applicants respectfully request withdrawal of this rejection.

Paragraph 12: The Examiner rejected claims 21, 22 and 26 as obvious over the Medicus reference in view of Riley et al. Applicants respectfully disagree. The Riley reference also fails to disclose a producing system, or make any suggestion of adaptability to that purpose. Thus, one of the limitations of independent claim 16 is missing when these two references are combined. As such, an element of the dependent claims 21, 22 and 23 is also missing. Applicants request withdrawal of this rejection.

Paragraph 13: The independent claims 16, 29 and 30 as well as dependent claims 17, 21, 22, 24, 25, 27 and 28 stand rejected under §103 as obvious over Kim et al. in view of Medicus et al. Again, Applicants respectfully disagree with this rejection.

There is no motivation to combine these two references. Neither reference indicates the desirability of such a combination. For example, the Medicus reference simply describes a dialysis system and never discusses or alludes to adaptability of this system for use as a bioreactor. Further, there is no indication that this system is specifically useful for protein synthesis reactions. The only indication is that the Medicus system is useful for dialysing compounds. Thus, the Medicus reference does not provide any impetus for a combination with the Kim reference.

In the Kim reference, there is absolutely no disclosure or suggestion of any advantage being conferred by a multiwell arrangement. There is no indication that the authors of the Kim reference contemplated a multiwell system as an improvement to their system. The Kim

reference only speaks generally and vaguely about future improvements, but provides no guidance that would point a reader to the multiwell arrangement disclosed by the present patent application, nor does it provide any guidance that would lead a reader to the Medicus reference specifically. Thus, the Kim reference fails to provide any impetus for the reader for a combination with the Medicus reference, and fails to provide any impetus for the specific improvement covered by the present patent application.

Applicants respectfully assert that the combination of the Kim and Medicus references is an example of prohibited "hind sight" examination. If one looks at the Kim and Medicus references without contemplation of the present patent application, one sees that there is no motivation to combine the references, nor is it obvious to make the improvement of having a multiwell bioreactor. The only motivation to combine these two references is provided by the present patent application. The Examiner may not consider that which is taught in the present patent application when making a rejection for obviousness under §103.

For these reasons, Applicants respectfully request that the rejections found in paragraph 13 of the pending Office Action be withdrawn. Applicants further point out that withdrawal of this rejection removes all obviousness-type rejections of the independent claims, and therefore obviates the remaining §103 rejections that cover the claims that depend therefrom.

Paragraph 14: Claims 21, 22, 26 and 30 stand rejected under §103 as being unpatentable over the Kim reference in view of the Medicus reference and Riley et al. Applicants respectfully disagree with this rejection.

As described above, there is no motivation to combine the Kim and Medicus references. The addition of the Riley reference to the equation does not change this lack of motivation. Riley, like Medicus, deals exclusively with an apparatus that gives no indication of usefulness as a bioreactor, or as a container for producing systems that result in the translation of proteins. There is no suggestion in Riley, Medicus or Kim of the adaptability of a multiwell apparatus for a bioreactor purpose. Because there is no suggestion to combine the references, and no suggestion of the desirability of the improvement of having a multiple well bioreactor, these references do

not render the present invention obvious. Applicants respectfully request withdrawal of the rejection.

Paragraph 15: Claim 23 was rejected as obvious over the Kim reference, in view of the Medicus reference and Alakhov et al. As stated above, the combination of Kim with Medicus does not render the present invention obvious. The addition of the Alakhov reference does not cure this deficiency in that it provides no motivation to combine references that render the invention obvious.

The Alakhov reference is cited only for the proposition that it is known to employ a semipermeable membrane with a pore size of 100 kD or less during protein synthesis. This additional information does not cure the defect as argued above: that there is no reason to combine the Kim and Medicus references. Thus, when all three of these references are taken together, the present invention is not obvious. Applicants request withdrawal of this rejection.

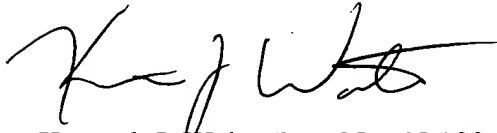
Paragraph 16: Claims 18-20 are rejected under §103 over the Kim reference in view of the Medicus reference and Rothschild. For the reasons stated above, the Kim and Medicus references cannot properly be combined to allow a holding of obviousness because these two references fail to motivate an inventor to perform such a combination. The addition of the Rothschild reference does not cure this defect, and there is no motivation to combine these three references.

Rothschild is only cited for the proposition that it is known in the art to immobilize streptavidin or avidin on a solid surface so as to isolate chemical, biochemical or biological materials. There is no teaching in Rothschild that would justify or provide motivation for combining the cited references; thus, this combination cannot render the present invention obvious. Withdrawal of the rejection is respectfully requested.

For the above-mentioned reasons, Applicants believe the claims as presently offered are in condition for allowance. Withdrawal of all rejections and allowance of the claims is

respectfully requested.

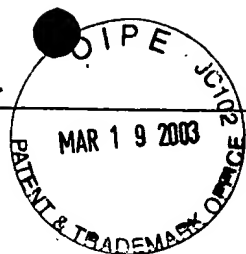
Respectfully submitted,



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16. (currently amended) A device for carrying out biochemical reactions for cell-free polypeptide biosynthesis and/or for the production of biologically active proteins, said device comprising an external housing that encloses an inner housing, said inner housing having incorporated wells and a supply chamber, wherein the wells of the inner housing each contain a producing system during the biochemical reaction, the supply chamber contains a supply liquid during the biochemical reaction and the wells of the inner housing and the supply chamber are separated by a one or more semipermeable membranes, the inner housing having at least two wells, the lower ends of which are closed by a said one or more semipermeable membranes and the upper ends of which protrude from the supply liquid contained in the supply chamber, connected to means for moving and incubating the producing systems and the supply liquid.
17. (previously added) The device of claim 16, wherein the inner housing has between 2 and about 1000 wells.

18. (previously added) The device of claim 16, wherein the wells have side walls that are coated with a component which specifically binds the in vitro synthesized proteins.
19. (previously added) The device of claim 18, wherein the wells are coated with components that are suitable for purifying polypeptides that bind to the components.
20. (previously added) The device of claim 18, wherein the wells are coated with streptactin, avidin or streptavidin.
21. (previously added) The device of claim 16, wherein the wells of the inner housing each have a volume between 50  $\mu$ l and 10 ml.
22. (previously added) The device of claim 16, wherein the volume of the supply solution is five to twenty-times the sum of the volumes of the wells.
23. (previously added) The device of claim 16, wherein the semipermeable membrane is a dialysis membrane or an ultrafiltration membrane with a pore size of 3 to 100 kDa.
24. (previously added) The device of claim 16 wherein the upper ends of the wells are sealed individually.
25. (previously added) The device of claim 16 wherein the outer housing is sealed with a closing cover.
26. (previously added) The device of claim 16, wherein the wells of the inner housing are composed of blocks having the same bore geometry and having a membrane fixed between the blocks.
27. (previously added) The device of claim 16, wherein the means for moving is configured such that the producing system and supply solution are mixed simultaneously.

28. (previously added) The device of claim 27, wherein the mixing is achieved by a shaking or stirring element.
29. (currently amended) A method for carrying out one or several biochemical reactions concurrently, ~~said method comprising~~ utilizing a device as claimed in claim 16, said method comprising supplying a supply liquid into a supply chamber, wherein the supply liquid in the supply chamber is not subjected to an external applied pressure during the biochemical reaction and thus the molecular exchange between the supply chamber and the individual wells of the inner housing is essentially based on diffusion.
30. (currently amended) A method for carrying out one or several biochemical reactions concurrently, ~~said method comprising~~ utilizing a device as claimed in as claimed in claim 26 or 27, said method comprising <sup>5</sup>supplying a supply liquid into a supply chamber, wherein the supply liquid and optionally the producing system in each of the wells of the inner housing are moved during the biochemical reaction by means of a magnetic stirring element.
31. (previously added) A kit comprising the following components: a solution comprising a substance buffering between pH 7 and 8, 150 to 400 mM potassium ions, 10 to 50 mM magnesium ions, nucleotide triphosphates, amino acids and a substance reducing sulfide groups; an energy-rich compound; a tRNA fraction; and optionally a RNA polymerase and/or a cell-free lysate.